? s bcl (w) 2 and inhibit? and py<1990

Processing
Processing
Processing
22516 BCL
4765502 2
19787 BCL(W)2
1852355 INHIBIT?
13325594 PY<1990
S1 1 BCL (W) 2 AND INHIBIT? AND PY<1990
? t s1/3,ab/all

1/3,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2001 Dialog Corporation. All rts. reserv.

05304798 89366239 PMID: 2771409
Regulation of **bcl-2** gene expression in lymphoid cell lines containing normal #18 or t(14;18) chromosomes.
Reed JC; Tsujimoto Y; Epstein SF; Cuddy M; Slabiak T; Nowell PC; Croce CM
Department of Pathology and Laboratory Medicine, University of Pennsylvania School of Medicine, Philadelphia 19104-6082.
Oncogene research (SWITZERLAND) **1989**, 4 (4) p271-82, ISSN 0890-6467 Journal Code: OND
Contract/Grant No.: CA39860, CA, NCI; CA42232, CA, NCI; CA47956, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The **bcl-2** (B cell lymphoma/leukemia-2) gene at band 18q21 is involved in t(14;18) chromosomal translocations in most follicular lymphomas and occasional other human B cell malignancies, where it becomes juxtaposed to the transcriptionally active immunoglobulin (Ig) locus at 14q32. Regulation of **bcl-2** gene expression was investigated in neoplastic lymphoid cell lines containing normal #18 chromosomes or a t(14;18) translocation with regard to steady-state mRNA levels, RNA stability, transcription rates, and DNA methylation. High steady-state levels of **bcl-2** mRNA, and proportionally high rates of **bcl-2** transcription (measured in isolated nuclei), were found in B cell lines containing t(14;18) translocations. The half-life of **bcl-2** mRNA (approximately 2-3 hr) was similar in all cell lines examined, including a t(14;18)-containing follicular lymphoma cell line, which has a translocated and rearranged **bcl-2** gene that produces **bcl-2**/Ig fusion transcripts. However, in the presence of cycloheximide (**inhibitor** of protein synthesis), the half-life of some of the **bcl-2** /Ig mRNAs produced by these cells was prolonged, indicating that in some circumstances mRNA stability may contribute to deregulated **bcl-2** expression. Despite stabilizing some **bcl-2** mRNAs, the overall effect of treating cell lines with cycloheximide was a reduction in the levels of accumulated **bcl-2** mRNAs through **inhibition** of **bcl-2** gene transcription. These latter data provide indirect evidence that short-lived transacting factor(s) regulate transcription of the human **bcl-2** gene in lymphoid cells with or without a t(14;18) translocation. No clear correlation was discovered between **bcl-2** gene methylation and transcription.
? s bcl(2) and clone? and py<1990

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             0  BCL(2)
        296569  CLONE?
      13325594  PY<1990
    S2        0  BCL(2) AND CLONE? AND PY<1990
? s bcl(w) 2 and clone? and py<1990

Processing
         22516  BCL
       4765502  2
         19787  BCL(W)2
        296569  CLONE?
      13325594  PY<1990
    S3       25  BCL(W) 2 AND CLONE? AND PY<1990
? rd

...completed examining records
    S4       17  RD (unique items)
? t s4/3,ab/all


 4/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2001 Dialog Corporation. All rts. reserv.

06412457   87242961   PMID: 3297209
  The gene located at chromosome 18 band q21 is rearranged in uncultured
diffuse lymphomas as well as follicular lymphomas.
  Lee MS; Blick MB; Pathak S; Trujillo JM; Butler JJ; Katz RL; McLaughlin P
; Hagemeister FB; Velasquez WS; Goodacre A; et al
  Blood (UNITED STATES)   Jul 1987,  70  (1)  p90-5,  ISSN 0006-4971
Journal Code: A8G
  Languages: ENGLISH
  Document type: Journal Article
  Record type: Completed
  The karyotypic abnormality t(14;18)(q32;q21) is reported to occur in 75%
of follicular lymphomas. This translocation results in the rearrangement of
a putative oncogene bcl-2, which resides at chromosome 18 band
q21 (the 18q21 gene). Using two human genomic DNA fragments cloned
from the chromosome 18 band q21 as probes, we analyzed 65 uncultured human
lymphoma samples by the Southern blot technique. The 18q21 gene was
rearranged in 18 of 26 (69%) follicular lymphomas, 3 of 5 (60%) follicular
lymphomas transformed to large cell lymphomas, 8 of 20 (40%) diffuse large
cell lymphomas (DLCLs), and 2 of 7 (29%) small noncleaved cell lymphomas
(SNCs). Our analysis detected rearrangement of the 18q21 gene in 10 of 13
(77%) cases in which the t(14;18)(q32;q21) translocation was found by
cytogenetic techniques. Our analysis also proved helpful in difficult
karyotyping situations: (a) identifying the donor chromosome fragment as
chromosome 18 band q21 in 4 of 9 (44%) cases that cytogenetically displayed
a 14q+ chromosome of unknown origin, and (b) identifying a rearrangement of
chromosome 18 band q21 in 12 of 18 (67%) cases that cytogenetically yielded
no cells in metaphase. We also demonstrated three cases of submicroscopic
rearrangement of the 18q21 gene. In our studies, patients with DLCLs and
rearrangement of the 18q21 gene had a significantly higher incidence of
extranodal involvement when compared with patients with DLCLs and no 18q21
gene rearrangement (P = 0.03).


 4/3,AB/2     (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2001 Dialog Corporation. All rts. reserv.

06179082   85244596   PMID: 3874430
  Involvement of the bcl-2 gene in human follicular lymphoma.
  Tsujimoto Y; Cossman J; Jaffe E; Croce CM
  Science (UNITED STATES)   Jun 21 1985,  228  (4706)  p1440-3,
```

ISSN 0036-8075 Journal Code: UJ7
Contract/Grant No.: C[redacted]685, CA, NCI; CA36521, CA, NCI[redacted]
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Recombinant DNA probes were **cloned** for the areas flanking the breakpoint on chromosome 18 in cells from a patient with acute lymphocytic leukemia of the B-cell type; cells of this line carry the t(14;18) chromosomal translocation. Two of the probes detected DNA rearrangements in approximately 60 percent of the cases of follicular lymphoma screened. In follicular lymphoma, most of the breakpoints in band q21 of chromosome 18 were clustered within a short stretch of DNA, approximately 2.1 kilobases in length. Chromosome 18-specific DNA probes for the areas flanking the breakpoints also detected RNA transcripts 6 kilobases in length in various cell types. The gene coding for these transcript (the **bcl-2** gene) seems to be interrupted in most cases of follicular lymphomas carrying the t(14;18) chromosomal translocation.

4/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2001 Dialog Corporation. All rts. reserv.

05976568 91170163 PMID: 2518688
The transgenic window on lymphoid malignancy.
Adams JM; Harris AW; Vaux DL; Alexander WS; Rosenbaum H; Klinken SP; Strasser A; Bath ML; McNeall J; Cory S
Walter and Eliza Hall Institute of Medical Research, Post Office Royal Melbourne Hospital, Victoria, Australia.
Princess Takamatsu symposia (UNITED STATES) **1989**, 20 p297-309, Journal Code: HHI
Contract/Grant No.: CA12421, CA, NCI; CA43540, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Transgenic mice bearing an oncogene targetted for expression in a specific tissue can reveal how that oncogene influences differentiation and help to delineate the pathways to malignancy. To explore lymphoid neoplasia, we have made strains of transgenic mice bearing different oncogenes driven by the immunoglobulin heavy chain enhancer (E mu), which promotes expression within lymphocytes and certain myeloid cells. The prototype E mu-myc mice succumb to pre-B and B cell lymphomas, following a preneoplastic phase in which cycling pre-B cells are overproduced. The similar fate of E mu-N-myc mice suggests that N-myc and myc have overlapping functions. Surprisingly, E mu-N-ras mice develop T lymphomas and macrophage tumours but no B lineage tumours; thus the ability of ras to initiate tumorigenesis may be lineage specific. Similarly, the high predisposition of E mu-v-abl mice to develop plasmacytomas may indicate that v-abl is oncogenic only at certain stages of B cell maturation. The **bcl-2** gene promotes cell survival rather than proliferation, and E mu-**bcl-2** mice produce copious resting B lymphocytes. The random onset and monoclonality of tumours in the transgenic strains argues for spontaneous genetic alterations that cooperate with the trans-oncogene. Indeed, most plasmacytomas of E mu-v-abl mice bear spontaneous myc rearrangements. Moreover, a minority of E mu-myc B lymphomas exhibit ras mutation, and the tumorigenesis can be reconstructed by crossing E mu-myc and E mu-ras mice, or by retroviral delivery of v-ras or v-raf, either in vitro or in vivo. To access novel cooperating oncogenes, we are using a retrovirus lacking an oncogene as an insertional mutagen. This approach should be applicable to any trans-oncogenic strain and help to delineate the genetic events that trigger malignant **clones**.

4/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

(c) format only 2001 Dialog Corporation. All rts. reserv.

05970456 89135885 PMID: 2492904
Nonrandom rearrangement of chromosome 14 at band q32.33 in human lymphoid malignancies with mature B-cell phenotype.
Nishida K; Taniwaki M; Misawa S; Abe T
Third Department of Medicine, Kyoto Prefectural University of Medicine, Japan.
Cancer research (UNITED STATES) Mar 1 **1989**, 49 (5) p1275-81, ISSN 0008-5472 Journal Code: CNF
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Chromosomes were studied in 61 patients with differentiated B-cell malignancies including 21 with non-Hodgkin's lymphoma (NHL), three with hairy cell leukemia (HCL), eight with Waldenstrom's macroglobulinemia (WM), and 29 with plasma cell disorder. Chromosomally abnormal **clones** were identified in 35 of 61 patients studied: all with NHL, all with HCL, three of eight with WM, and eight of 29 with plasma cell disorder. The most recurrent chromosomal abnormality, observed in 26 of the 35 patients whose chromosomes were abnormal, was a rearrangement involving chromosome 14, in which an additional segment was attached at band 32 in the long arm to form a 14q+ marker chromosome. This rearrangement was seen in 17 patients with NHL, three with HCL, one with WM, and five with plasma cell disorder. In NHL, the rearrangement correlates with histological subclasses: t(14;18) in all four patients with malignant lymphoma (ML)-follicular, mixed small cleaved and large cell; t(8;14) or its variant form, t(8;22), in all six with ML-small noncleaved cell; and t(11;14) in two of three with ML-diffuse, mixed small and large cell. A t(14;18) was also found in each patient with ML-diffuse, large cell, WM, and multiple myeloma, and a variant three-way translocation, t(5;18;14) (q13;q21;q32), in one with ML-diffuse, small cleaved cell. The donor sites for these 14q+ were assigned to oncogene loci: c-myc (8q24), bcl-1 (11q13), and **bcl-2** (18q21). Moreover, the donor sites were also located near immunoglobulin light chain gene loci in each patient with leukemic ML-diffuse, mixed small and large cell, t(2;14) (p13;q32.3), and HCL, t(14;22)(q32.3;q11.2). These findings suggest that chimeric DNA formation, not only between an immunoglobulin gene and a certain oncogene, but also between the IgH gene and one of the IgL genes may be potentially relevant in malignant B-cell proliferation.

4/3,AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2001 Dialog Corporation. All rts. reserv.

05916634 88233652 PMID: 3131717
Pre-B-cell leukemia with a t(8; 14) and a t(14; 18) translocation is preceded by follicular lymphoma.
Gauwerky CE; Hoxie J; Nowell PC; Croce CM
Wistar Institute, Philadelphia, Pennsylvania 19104.
Oncogene (ENGLAND) May **1988**, 2 (5) p431-5, ISSN 0950-9232 Journal Code: ONC
Contract/Grant No.: CA 15822, CA, NCI; CA 39860, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We have performed gene rearrangement studies on the leukemic blasts of a patient with acute pre-B-cell leukemia. The patient had a 5 year history of follicular lymphoma, which developed into acute pre-B-cell leukemia. The leukemic blasts revealed a karyotype with two translocations, t(8; 14) and t(14; 18), characteristic for Burkitt's lymphoma and follicular lymphoma. The cells are TdT positive, do not possess surface immunoglobulin, and they show immunoglobulin gene rearrangement. The mu heavy chain and kappa light chain constant (C mu and C kappa) loci are deleted, while the gamma and

lambda light chain constant (C gamma and C lambda) region genes are rearranged. Both alleles of the heavy chain joining segment (JH) are rearranged on chromosome 14q+, one of them with the **bcl-2** oncogene from chromosome 18. The breakpoint of the t(14; 18) translocation occurs in the major breakpoint cluster region in the 3' untranslated region of **bcl-2** . On chromosome 8 a c-myc rearrangement was mapped immediately 5' to the c-myc first exon in a region involved in sporadic Burkitt lymphoma. The data are consistent with our previous hypothesis on the evolution of B-cell malignancies: a rare pre-B cell develops a t(14; 18) translocation during immunoglobulin VDJ joining that results in an expansion of a follicular lymphoma **clone** carrying an activated **bcl-2** gene. Within the **clone** of pre-B cells a second translocation, t(8; 14), occurs during heavy chain isotype switching that results in the deregulation of the c-myc involved in the translocation.

4/3,AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2001 Dialog Corporation. All rts. reserv.

05851404 89282816 PMID: 2543982
Growth- and tumor-promoting effects of deregulated BCL2 in human B-lymphoblastoid cells.
Nunez G; Seto M; Seremetis S; Ferrero D; Grignani F; Korsmeyer SJ; Dalla-Favera R
Department of Medicine, Howard Hughes Medical Institute, Washington University School of Medicine, Saint Louis, MO 63110.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Jun **1989**, 86 (12) p4589-93, ISSN 0027-8424 Journal Code: PV3
Contract/Grant No.: CA-37165, CA, NCI; T32 CAO 9547, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Human follicular B-cell lymphomas possess a t(14;18) that translocates a putative protooncogene, BCL2, into the immunoglobulin heavy chain locus. The normal BCL2 gene is quiescent in resting B cells, expressed in proliferating, but down-regulated in differentiated B cells. Inappropriately high levels of BCL2-immunoglobulin chimeric RNA are present in t(14;18) lymphomas for their mature B-cell stage. We examined the biologic effects of BCL2 deregulation in human B cells by introducing BCL2 into human B-lymphoblastoid cell lines (LCLs) with retroviral gene transfer. Although deregulated BCL2 expression as a single agent was not sufficient to confer tumorigenicity to LCLs, it consistently produced a 3- to 4-fold increment in LCL clonogenicity in soft agar. In addition, BCL2 deregulation complements the transforming effects of the MYC oncogene in LCLs. BCL2 augmented the clonogenicity of LCLs bearing exogenous MYC and increased the frequency and shortened the latency of tumor induction in immunodeficient mice. These results demonstrate a role for BCL2 as a protooncogene that affects B-cell growth and enhances B-cell neoplasia.

4/3,AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2001 Dialog Corporation. All rts. reserv.

05817282 87002488 PMID: 2875799
Cloning and structural analysis of cDNAs for **bcl-2** and a hybrid **bcl-2** /immunoglobulin transcript resulting from the t(14;18) translocation.
Cleary ML; Smith SD; Sklar J
Cell (UNITED STATES) Oct 10 **1986**, 47 (1) p19-28, ISSN 0092-8674 Journal Code: CQ4
Contract/Grant No.: CA34233, CA, NCI; CA38621, CA, NCI
Languages: ENGLISH

Document type: Journal Article
Record type: Complete

cDNAs for the **bcl-2** mRNA were **cloned** from a human common acute lymphoblastic leukemia cell line. Nucleotide sequence analyses showed that the 6 kb **bcl-2** mRNA potentially encodes a 26 kd protein that is homologous to a predicted Epstein-Barr virus protein. Most t(14;18) translocation breakpoints cluster within a narrow region of a 5.4 kb exon that contains a long 3'-untranslated region of the **bcl-2** mRNA. As a result of t(14;18) translocation, hybrid **bcl-2**/immunoglobulin heavy chain transcripts are produced that consist of the 5' half of the **bcl-2** mRNA fused to a "decapitated" immunoglobulin heavy chain mRNA. Nucleotide sequence analyses confirmed that the hybrid transcripts continue to encode a normal **bcl-2** protein. Our results suggest that t(14;18) translocations alter expression of the **bcl-2** gene both by transcriptional activation and by abnormal posttranscriptional regulation of **bcl-2** mRNA.

4/3,AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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05767970 87187643 PMID: 3032455

Molecular analysis of mbcl-2: structure and expression of the murine gene homologous to the human gene involved in follicular lymphoma.

Negrini M; Silini E; Kozak C; Tsujimoto Y; Croce CM

Cell (UNITED STATES) May 22 **1987**, 49 (4) p455-63, ISSN 0092-8674 Journal Code: CQ4

Contract/Grant No.: 1, U41, RR-01685-03, RR, NCRR

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

We have **cloned** the mouse **bcl-2** (mbcl-2) genomic locus and analyzed it in detail. The gene is comprised of two exons separated by more than 15 kb. Two species of mRNAs are produced, and DNA sequencing analysis shows that they code for two proteins differing at their C terminus: a 7.5 kb transcript codes for a polypeptide of 236 amino acids, mbcl-2 alpha, and a 2.4 kb transcript, which derives from the 5' exon only, codes for a protein of 199 amino acids, mbcl-2 beta. The gene is characterized by very long (5' about 1.4 kb, and 3' about 5.1 kb) untranslated regions surrounding the relatively short coding region. We have mapped the 5' end of the mbcl-2 mRNAs by S1 protection analysis, and we have analyzed the promoter region. The expression of the mbcl-2 gene was analyzed in different cell lines and in mouse tissues. Expression is tissue-specific in adult tissues: spleen and thymus express the highest level of mbcl-2 transcripts. The mbcl-2 gene maps to mouse chromosome 1.

4/3,AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2001 Dialog Corporation. All rts. reserv.

05764827 87321098 PMID: 2820125

Identification of an Epstein-Barr virus early gene encoding a second component of the restricted early antigen complex.

Pearson GR; Luka J; Petti L; Sample J; Birkenbach M; Braun D; Kieff E

Virology (UNITED STATES) Sep **1987**, 160 (1) p151-61, ISSN 0042-6822 Journal Code: XEA

Contract/Grant No.: CA-09241, CA, NCI; CA-17281, CA, NCI; CA-39617, CA, NCI; +

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

When the latent Epstein-Barr virus (EBV) genome in B95-8 cells is induced into a replicative phase, two abundant early RNAs are transcribed rightward

from the EBV BamHI H DNA fragment into BamHI F. Analysis of cDNA **clones** prepared from [redacted] RNA of cells replicating EBV [redacted] revealed that both RNAs contain the BHRF1 open reading frame. Part of BHRF1, **cloned** into a prokaryotic fusion protein expression vector, expressed a fusion protein in Escherichia coli and the purified fusion protein was used to generate a monoclonal antibody against BHRF1. This antibody was then employed to characterize the protein encoded by BHRF1 in cells replicating EBV. The monoclonal antibody reacted with a 17-kDa protein component of the restricted early antigen (EA) complex. The distribution of the protein in cells was similar to that noted when sera from patients with African Burkitt's lymphoma were used to stain these cells. The protein was synthesized before the major 47-56 kDa protein associated with the diffuse component of EA in superinfected Raji cells. All human sera containing antibodies to EA as determined by immunofluorescence (IF) reacted with the protein as did some sera determined to be anti-VCA positive and anti-EA negative by IF. The predicted amino acid sequence of the protein has characteristics which suggest that it is a membrane protein. It also has significant homology with both the anchor region of polyoma middle T antigen and with the predicted protein product of the **bcl-2** mRNA activated by the 14/18 chromosome translocation characteristic of follicular lymphomas. This latter homology is extensive and colinear, suggesting common evolution and function. However, neither a mRNA which could efficiently translate the BHRF1 protein nor the BHRF1 protein could be detected in latently infected cells. Thus, the **bcl-2** predicted protein is similar to an EBV protein synthesized in the early phase of virus infection.

4/3,AB/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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05758769 87187114 PMID: 3032407
Clonal evolution of t(14;18) follicular lymphomas demonstrated by immunoglobulin genes and the 18q21 major breakpoint region.
Raffeld M; Wright JJ; Lipford E; Cossman J; Longo DL; Bakhshi A; Korsmeyer SJ
Cancer research (UNITED STATES) May 15 **1987**, 47 (10) p2537-42, ISSN 0008-5472 Journal Code: CNF
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A 2.8-kilobase major breakpoint region on chromosome segment 18q21 is the site of most t(14;18) translocations typical of human follicular lymphomas. Breaks are focused at the 5' end of joining (JH) regions of immunoglobulin (Ig) on chromosome 14, indicating that the translocation occurs at a pre-B-cell stage during attempted heavy (H) chain joining. A new gene from 18q21 (**Bcl-2**) is placed in the H chain locus creating a unique, translocation-specific JH;18q21 rearrangement that presumably represents a transformation event. In addition, normal Ig gene joining occurs in a H before light (L) chain and K before lambda cascade, creating ordered clonal markers. These serial markers were examined to determine if variations in Ig gene patterns during the natural history of lymphomas represent the emergence of truly separate neoplasms or heterogeneity of a single neoplasm. We examined 45 serial biopsies from 16 B follicular lymphoma patients; six cases showed variation in Ig gene patterns over time. Seven individuals had a detectable JH;18q21 rearrangement present, and it remained unchanged over 5-10 years. Further rearrangements of H chain genes occurred on the normal chromosome 14 within evolving subclones of the original tumor. Lambda L chains also underwent additional rearrangements in two instances, while K gene patterns remained unchanged. All variations in the normal H and L chain genes were 2 degrees rearrangements occurring at a mature B-cell stage following the initial successful rearrangement of a H and L chain. In contrast the t(14;18) breakpoint was conserved in each individual, indicating that evolving neoplastic subpopulations arose from a

common clonal progenitor cell.

4/3,AB/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2001 Dialog Corporation. All rts. reserv.

05632075 87190702 PMID: 3106072
Expression of the **bcl-2** gene in mouse B lymphocytic cell lines is differentiation stage specific.
Gurfinkel N; Unger T; Givol D; Mushinski JF
European journal of immunology (GERMANY, WEST) Apr **1987**, 17 (4) p567-70, ISSN 0014-2980 Journal Code: EN5
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
cDNA **clones** of mouse **bcl-2** have been isolated and characterized by homology to the human **bcl-2** gene, a putative oncogene that is found on the portion of chromosome 18 characteristically involved in the t(14;18) translocation present in nearly all human follicular B cell lymphomas. Our mouse cDNA **clone** detects 7.9 and 6.3-kb **bcl-2** RNAs in mouse B cell lymphomas, but only in tumors consisting of pre-B and follicular center mature B cells, not in pro-B cell or plasma cell tumors. Thus, this gene appears to be a B cell differentiation marker that is expressed only in committed B cells, but is shut off in end stage plasma cells. This pattern of expression is unique among oncogenes, and we suggest that it may be responsible for the high frequency of translocations at this locus in the common malignancy of human mature B cells, follicular lymphomas.

4/3,AB/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2001 Dialog Corporation. All rts. reserv.

05570812 88217344 PMID: 3285301
Consequences of the t(14;18) chromosomal translocation in follicular lymphoma: deregulated expression of a chimeric and mutated **BCL-2** gene.
Hua C; Zorn S; Jensen JP; Coupland RW; Ko HS; Wright JJ; Bakhshi A
Metabolism Branch, National Institutes of Health, Bethesda, MD 20892.
Oncogene research (SWITZERLAND) Feb **1988**, 2 (3) p263-75, ISSN 0890-6467 Journal Code: OND
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The t(14;18) chromosomal translocation of human follicular lymphoma recombines the candidate transforming gene **bcl-2**, located at 18q21, with the immunoglobulin (Ig) H-chain joining region (JH) at 14q32. To elucidate the consequences of this translocation, we **cloned** **bcl-2** cDNAs from a pre-B cell line (Nall-1) and a t(14;18) lymphoma cell line (SU-DHL-6) and compared these sequences with their genomic counterparts. These studies revealed the complexity of **bcl-2** gene expression in which six potential polyadenylation signals in exon 3 and two different 5' exons (exons 1 and 2) and promoters are alternatively used to generate different sized **bcl-2** mRNAs. A single open reading frame (ORF), at the junction of exons 2 and 3, predicts a 239 amino acid, 26 kD protein. Most chromosome 18 breakpoints cluster within a 150 bp region of exon 3. In SU-DHL-6 the t(14;18) translocation juxtaposes a truncated **bcl-2** gene with J6 in a tail-to-head configuration, resulting in the deregulated expression of chimeric **bcl-2**/Ig transcripts. Importantly, the SU-DHL-6 **bcl-2** cDNA also contained several point mutations in the ORF, two of which altered the primary amino acid sequence. The deregulated expression of an altered **bcl-2** gene may play a critical role in the

disordered growth and differentiation of follicular B cell lymphoma.

4/3,AB/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2001 Dialog Corporation. All rts. reserv.

05253479 88334725 PMID: 3262202
Bcl-2 gene promotes haemopoietic cell survival and cooperates with c-myc to immortalize pre-B cells.
Vaux DL; Cory S; Adams JM
Walter and Eliza Hall Institute of Medical Research, PO Royal Melbourne Hospital, Victoria, Australia.
Nature (ENGLAND) Sep 29 **1988**, 335 (6189) p440-2, ISSN 0028-0836 Journal Code: NSC
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A common feature of follicular lymphoma, the most prevalent haematological malignancy in humans, is a chromosome translocation (t(14;18] that has coupled the immunoglobulin heavy chain locus to a chromosome 18 gene denoted **bcl-2** . By analogy with the translocated c-myc oncogene in other B-lymphoid tumours **bcl-2** is a candidate oncogene, but no biological effects of **bcl-2** have yet been reported. To test whether **bcl-2** influences the growth of haematopoietic cells, either alone or together with a deregulated c-myc gene, we have introduced a human **bcl-2** complementary DNA using a retroviral vector into bone marrow cells from either normal or E mu-myc transgenic mice, in which B-lineage cells constitutively express the c-myc gene. **Bcl-2** cooperated with c-myc to promote proliferation of B-cell precursors, some of which became tumorigenic. To determine how **bcl-2** expression impinges on growth factor requirements, the gene was introduced into a lymphoid and a myeloid cell line that require interleukin 3 (IL-3). In the absence of IL-3, **bcl-2** promoted the survival of the infected cells but they persisted in a G0 state, rather than proliferating. These results argue that **bcl-2** provided a distinct survival signal to the cell and may contribute to neoplasia by allowing a **clone** to persist until other oncogenes, such as c-myc, become activated.

4/3,AB/14 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2001 Dialog Corporation. All rts. reserv.

05166141 86259760 PMID: 3523487
Analysis of the structure, transcripts, and protein products of **bcl-2**, the gene involved in human follicular lymphoma.
Tsujimoto Y; Croce CM
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Jul **1986**, 83 (14) p5214-8, ISSN 0027-8424 Journal Code: PV3
Contract/Grant No.: CA39860, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We have determined that the **bcl-2** (B-cell leukemia/lymphoma 2) gene is transcribed into three overlapping mRNAs, and we have **cloned** **bcl-2** cDNA sequences. Sequence analysis of the **bcl-2** cDNA **clones** and comparison of their sequences to their genomic counterparts indicate that the **bcl-2** gene contains at least two exons. The three **bcl-2** transcripts, which are 8.5, 5.5, and 3.5 kilobases (kb) long, overlap within the first exon, but only the 8.5-kb and 5.5-kb transcripts contain sequences of the second exon. The 8.5-kb and 5.5-kb transcripts seem to use different

polyadenylylation sites. Sequence analysis of the cDNA **clones** corresponding to the [redacted].5-kb and 3.5-kb mRNAs indicates that the two **bcl-2** transcripts carry two overlapping open reading frames, one of which is 717 nucleotides long and codes for a protein (**bcl-2** alpha) of 239 amino acids and a molecular mass of 26 kDa, while the other codes for a protein of 205 amino acids (**bcl-2** beta, molecular mass 22 kDa) that is identical to **bcl-2** alpha except at the carboxyl terminus. The **bcl-2** protein products in follicular lymphomas with or without **bcl-2** rearrangements are identical to the normal **bcl-2** products.

4/3,AB/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2001 Dialog Corporation. All rts. reserv.

04994657 85213848 PMID: 3923362
Clustering of breakpoints on chromosome 11 in human B-cell neoplasms with the t(11;14) chromosome translocation.
Tsujimoto Y; Jaffe E; Cossman J; Gorham J; Nowell PC; Croce CM
Nature (ENGLAND) May 23-29 **1985**, 315 (6017) p340-3, ISSN 0028-0836 Journal Code: NSC
Contract/Grant No.: CA15822, CA, NCI; CA16685, CA, NCI; CA36521, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
The t(11;14) (q13;q32) chromosome translocation has been reported in diffuse small and large cell lymphomas and in chronic lymphocytic leukaemia (B-CLL) and multiple myeloma. Because chromosome band 14q32 is involved in this translocation, as well as in the t(8;14) (q24;q32) translocation of the Burkitt tumour, interruption of the immunoglobulin heavy-chain locus was postulated for this rearrangement. We have **cloned** the chromosomal joinings between chromosomes 11 and 14 and also between chromosomes 14 and 18, in B-cell tumours carrying translocations involving these chromosomes, and suggested the existence of two translocated loci, bcl-1 and **bcl-2**, normally located on chromosomes 11 (band q13) and 18 (band q21) respectively, involved in the pathogenesis of human B-cell neoplasms. The results indicate that in the leukaemic cells from two different cases of CLL, the breakpoints on chromosome 11 are within 8 nucleotides of each other and on chromosome 14 involve the J4-DNA segment. Because we detected a 7mer-9mer signal-like sequence with a 12-base-long spacer on the normal chromosome 11, close to the breakpoint, we speculate that the t(11;14) chromosome translocation in CLL may be sequence specific and may involve the recombination system for immunoglobulin gene segment (V-D-J) joining.

4/3,AB/16 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
(c) 2001 BIOSIS. All rts. reserv.

05552308 BIOSIS NO.: 000083025448
CLONING AND STRUCTURAL ANALYSIS OF COMPLEMENTARY DNA FOR **BCL-2** AND A HYBRID **BCL-2**-IMMUNOGLOBULIN TRANSCRIPT RESULTING FROM THE 14 18 TRANSLOCATION
AUTHOR: CLEARY M L; SMITH S D; SKLAR J
AUTHOR ADDRESS: LAB. OF EXPERIMENTAL ONCOL., DEP. OF PATHOL. STANFORD, CALIFORNIA 94305.
JOURNAL: CELL 47 (1). 1986. 19-28. **1986**
FULL JOURNAL NAME: Cell
CODEN: CELLB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: cDNAs for the **bcl-2** mRNA were **cloned** from a human common acute lymphoblastic leukemia cell line. Nucleotide sequence

analyses showed that the 6 kb **bcl-2** mRNA potentially encodes a 26 kd progein that is homologous to a predicted Epstein-Barr virus protein. Most t(14;18) translocation breakpoints cluster within a narrow region of 5.4 kb exon that contains a long 3'-untranslated region of the **bcl-2** mRNA. As a result of t(14;18) translocation, hybrid **bcl-2**/immunoglobulin heavy chain transcripts are produced that consist of the 5' half of the **bcl-2** mRNA fused to a "decapitated" immunoglobulin heavy chain mRNA. Nucleotide sequence analyses confirmed that the hybrid transcripts continue to encode a normal **bcl-2** protein. Our results suggest that t(14;18) translocations after expression of the **bcl-2** gene both by transcriptional activation and by abnormal posttranscriptional regulation of **bcl-2** mRNA.

1986

4/3,AB/17 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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04619465 BIOSIS NO.: 000079032502
CHROMOSOME TRANSLOCATIONS AND B CELL NEOPLASIA
AUTHOR: CROCE C M; TSUJIMOTO Y; ERIKSON J; NOWELL P
AUTHOR ADDRESS: WISTAR INST. ANATOMY BIOL., 36TH AND SPRUCE ST., PHILADELPHIA, 19104 PA. USA.
JOURNAL: LAB INVEST 51 (3). 1984. 258-267. **1984**
FULL JOURNAL NAME: Laboratory Investigation
CODEN: LAINA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Other B cell lymphomas and leukemias of adults as well as the c-myc oncogene of Burkitt's lymphoma are studied. There are indications that 2 additional loci, bcl-1 and **bcl-2**, may have an important role in the pathogenesis of these diseases. By using recombinant DNA technologies, these 2 loci were **cloned** and their rearrangements in B cell neoplasms carrying either the t(11;14) or the t(14;18) chromosome translocation were observed. The availability of these probes should allow investigation of the structure, organization and expression of these loci and of their role in human tumors. It should also lead to further understanding of the mechanisms of gene activation in neoplastic B cells. The molecular approach to specific chromosomal translocations is opening new avenues to probe the genetic mechanisms of carcinogenesis.

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? b 155, 5

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*File 155: This file has been reloaded. Accession numbers have changed.
 Please see Help News155 for further details.
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            5102  RIBOZYM?
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            5102  RIBOZYM?
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 3/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2001 Dialog Corporation. All rts. reserv.

07833584   91301181   PMID: 2070813
  Mitochondrial protein p26 BCL2 reduces growth factor requirements of
NIH3T3 fibroblasts.
  Reed JC; Talwar HS; Cuddy M; Baffy G; Williamson J; Rapp UR; Fisher GJ
  University of Pennsylvania School of Medicine, Department of Pathology
and Laboratory Medicine, Philadelphia 19104.
  Experimental cell research (UNITED STATES)  Aug 1991,  195  (2)
 p277-83,  ISSN 0014-4827   Journal Code: EPB
  Contract/Grant No.: AR39691, AR, NIAMS; CA49576, CA, NCI; FO5DW04545, PHS
; +
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Languages: ENGLISH
Document type: Journal Article
Record type: Completed

The BCL2 (B cell lymphoma/leukemia-2) proto-oncogene encodes a 26-kDa protein that has been localized to the inner mitochondrial membrane and that has been shown to enhance the survival of some types of hematopoietic cells. Here we show that NIH3T3 fibroblasts stably transfected with a BCL2 expression plasmid exhibit reduced dependence on competence-inducing growth factors (platelet-derived growth factor, PDGF; epidermal growth factor, EGF) for initiation of DNA synthesis. The importance of BCL2 for growth factor-induced proliferation of these cells was further confirmed by the useage of BCL2 **antisense** oligodeoxynucleotides. The mechanisms by which overexpression of p26 BCL2 contributes to fibroblast proliferation are unknown, but do not involve alterations in: (a) the production of inositol triphosphates (IP3), (b) PDGF-induced transient elevations in cytosolic Ca2+ ions, or (c) the activity of protein kinase C enzymes in these transfected cells. The results imply that changes in mitochondrial functions play an important role in the early stages of the cell cycle that render 3T3 cells competent to respond to the serum progression factors that stimulate entry into S-phase.

3/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2001 Dialog Corporation. All rts. reserv.

07735703 91004004 PMID: 2208117

Antisense-mediated inhibition of BCL2 protooncogene expression and leukemic cell growth and survival: comparisons of phosphodiester and phosphorothioate oligodeoxynucleotides.

Reed JC; Stein C; Subasinghe C; Haldar S; Croce CM; Yum S; Cohen J
Department of Pathology, University of Pennsylvania School of Medicine, Philadelphia 19104-6082.

Cancer research (UNITED STATES) Oct 15 **1990**, 50 (20) p6565-70, ISSN 0008-5472 Journal Code: CNF
Contract/Grant No.: CA-47946, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Antisense oligodeoxynucleotides specific for sequences in mRNAs from the B-cell lymphoma/leukemia-2 (BCL2) gene were used to inhibit the growth in culture of a human leukemia cell line, 697. Normal phosphodiester (PO) and nuclease-resistant phosphorothioate (PS) oligodeoxynucleotides were compared with regard to specificity, potency, and kinetics. Both PO and PS **antisense** BCL2 oligodeoxynucleotides were specific inhibitors of cellular proliferation, since sense versions of these synthetic DNAs were inactive at similar concentrations. Specificity was further confirmed by quantitative immunofluorescence studies, showing that PO and PS **antisense** BCL2 oligodeoxynucleotides (when used at appropriate concentrations) reduced levels of BCL2 protein without influencing expression of HLA-DR and other control antigens. The onset of inhibition by PO oligodeoxynucleotides was faster, with reductions in cell numbers occurring within 1 day of addition to cultures, in contrast to phosphorothioates, which were ineffective until 3-4 days. Phosphorothioates were more potent that phosphodiesters, however, with half-maximal inhibition of leukemic cell growth occurring at concentrations 5-10 times lower. As expected from previous studies demonstrating the importance of BCL2 for regulating lymphoid cell survival, BCL2 **antisense** oligodeoxynucleotides also led to 697 leukemic cell death through sequence-specific mechanisms, with reductions in cellular viability generally lagging the inhibitory effects on cellular growth by about 2 days. Taken together, these data indicate that PO and PS oligodeoxynucleotides targeted against the human BCL2 protooncogene can be sequence-specific inhibitors of leukemic cell growth and survival.

? s b(w)cell and (lymphoma or leukemia (w)2) and (antisens? or ribozyme?) and py<1992

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 5/3,AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2001 Dialog Corporation. All rts. reserv.

07833584   91301181   PMID: 2070813
  Mitochondrial protein p26 BCL2 reduces growth factor requirements of
NIH3T3 fibroblasts.
  Reed JC; Talwar HS; Cuddy M; Baffy G; Williamson J; Rapp UR; Fisher GJ
  University of Pennsylvania School of Medicine, Department of Pathology
and Laboratory Medicine, Philadelphia 19104.
  Experimental cell research (UNITED STATES)  Aug 1991,  195  (2)
 p277-83,  ISSN 0014-4827   Journal Code: EPB
  Contract/Grant No.: AR39691, AR, NIAMS; CA49576, CA, NCI; FO5DW04545, PHS
; +
  Languages: ENGLISH
  Document type: Journal Article
  Record type: Completed
  The BCL2 (B cell lymphoma/leukemia-2 )
proto-oncogene encodes a 26-kDa protein that has been localized to the
inner mitochondrial membrane and that has been shown to enhance the
survival of some types of hematopoietic cells. Here we show that NIH3T3
fibroblasts stably transfected with a BCL2 expression plasmid exhibit
reduced dependence on competence-inducing growth factors (platelet-derived
growth factor, PDGF; epidermal growth factor, EGF) for initiation of DNA
synthesis. The importance of BCL2 for growth factor-induced proliferation
of these cells was further confirmed by the useage of BCL2 antisense
oligodeoxynucleotides. The mechanisms by which overexpression of p26 BCL2
contributes to fibroblast proliferation are unknown, but do not involve
alterations in: (a) the production of inositol triphosphates (IP3), (b)
PDGF-induced transient elevations in cytosolic Ca2+ ions, or (c) the
activity of protein kinase C enzymes in these transfected cells. The
results imply that changes in mitochondrial functions play an important
role in the early stages of the cell cycle that render 3T3 cells competent
to respond to the serum progression factors that stimulate entry into
S-phase.


 5/3,AB/2     (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2001 Dialog Corporation. All rts. reserv.

07735703   91004004   PMID: 2208117
   Antisense-mediated inhibition of BCL2 protooncogene expression and
leukemic cell growth and survival: comparisons of phosphodiester and
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phosphorothioate oligod[redacted]xynucleotides.
Reed JC; Stein C; Su[redacted]inghe C; Haldar S; Croce CM; Yu[redacted]; Cohen J
Department of Pathology, University of Pennsylvania School of Medicine, Philadelphia 19104-6082.
Cancer research (UNITED STATES) Oct 15 **1990**, 50 (20) p6565-70, ISSN 0008-5472 Journal Code: CNF
Contract/Grant No.: CA-47946, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Antisense oligodeoxynucleotides specific for sequences in mRNAs from the **B-cell lymphoma/leukemia-2** (BCL2) gene were used to inhibit the growth in culture of a human leukemia cell line, 697. Normal phosphodiester (PO) and nuclease-resistant phosphorothioate (PS) oligodeoxynucleotides were compared with regard to specificity, potency, and kinetics. Both PO and PS **antisense** BCL2 oligodeoxynucleotides were specific inhibitors of cellular proliferation, since sense versions of these synthetic DNAs were inactive at similar concentrations. Specificity was further confirmed by quantitative immunofluorescence studies, showing that PO and PS **antisense** BCL2 oligodeoxynucleotides (when used at appropriate concentrations) reduced levels of BCL2 protein without influencing expression of HLA-DR and other control antigens. The onset of inhibition by PO oligodeoxynucleotides was faster, with reductions in cell numbers occurring within 1 day of addition to cultures, in contrast to phosphorothioates, which were ineffective until 3-4 days. Phosphorothioates were more potent that phosphodiesters, however, with half-maximal inhibition of leukemic cell growth occurring at concentrations 5-10 times lower. As expected from previous studies demonstrating the importance of BCL2 for regulating lymphoid cell survival, BCL2 **antisense** oligodeoxynucleotides also led to 697 leukemic cell death through sequence-specific mechanisms, with reductions in cellular viability generally lagging the inhibitory effects on cellular growth by about 2 days. Taken together, these data indicate that PO and PS oligodeoxynucleotides targeted against the human BCL2 protooncogene can be sequence-specific inhibitors of leukemic cell growth and survival.

5/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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06833487 90251616 PMID: 1692620
BCL2-mediated tumorigenicity of a human T-lymphoid cell line: synergy with MYC and inhibition by BCL2 **antisense**.
Reed JC; Cuddy M; Haldar S; Croce C; Nowell P; Makover D; Bradley K
Department of Pathology, University of Pennsylvania School of Medicine, Philadelphia 19104-6082.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) May **1990**, 87 (10) p3660-4, ISSN 0027-8424 Journal Code: PV3
Contract/Grant No.: CA42232, CA, NCI; CA47956, CA, NCI
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

A gene-transfer approach was used to explore the function of the BCL2 (**B-cell lymphoma/leukemia 2**) gene in a human T-cell line, Jurkat. Though stable introduction of a BCL2 expression plasmid into Jurkat T cells was by itself insufficient, the combined transfer of BCL2 and MYC genes markedly enhanced the tumorigenicity of these cells in athymic mice. Moreover, a BCL2 **antisense** expression plasmid ablated tumor formation by Jurkat cells, providing further evidence that this oncogene contributes to the regulation of the in vivo growth of these human T lymphocytes. In addition to their influence on tumor formation, BCL2 sense and **antisense** expression plasmids increased and decreased, respectively, the in vitro survival of Jurkat T cells in

serum-free medium. These observations extend to T cells the finding of synergy of BCL2 with MYC previously reported for B cells and provide evidence that BCL2 can regulate the growth of human T cells.

5/3,AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2001 Dialog Corporation. All rts. reserv.

05523434 91137515 PMID: 2562157
Specific inhibition of class II MHC gene expression by anti-sense RNA.
Hatano M; Aizawa S; Soejima T; Shigemoto K; Taniguchi M; Tokuhisa T
Department of Immunology, ICMR, Kobe University School of Medicine, Japan.
International immunology (ENGLAND) **1989**, 1 (3) p260-6, ISSN 0953-8178 Journal Code: AY5
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
We have established an anti-sense RNA system which is capable of regulating expression of the class II (Ia) molecule coded for by the major histocompatibility complex in cultured mouse cells. Various areas of the I-A beta chain gene were subcloned in an anti-sense orientation to the 3' of the dihydrofolate reductase (DHFR) cDNA under the control of the human metallothionein IIa gene promoter. These anti-sense DNA constructs were transfected into M12.4 cells, a BALB/c B **lymphoma** cell line which expresses both I-A and I-E molecules on the cell surface. I-A expression of selected clones transfected with anti-sense DNA encompassing the 5' untranslated region (UT) (100 or 310 bp) including the translation start site or the poly(A) addition signalling sequence in the 3' UT (250 bp) of the I-A beta chain gene were specifically reduced to less than 5% of the control M12.4 cell surface I-A expression. These clones had normal levels of I-E expression. However, transfection of the anti-sense DNA to the beta 1 domain (510 bp) including the splicing donor and acceptor sequences did not affect the expression of I-A molecules. The same **antisense** DNA constructs (100 bp of the 5' UT or 250 bp of the 3' UT) without the DHFR cDNA (710 bp) did not down-regulate the expression of I-A molecules, indicating that either the physical length of the anti-sense RNA or specific DHFR cDNA sequences are also important.(ABSTRACT TRUNCATED AT 250 WORDS)

5/3,AB/5 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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06766346 BIOSIS NO.: 000088075779
IG V REGION GENE EXPRESSION IN SMALL LYMPHOCYTIC **LYMPHOMA** WITH LITTLE OR NO SOMATIC HYPERMUTATION
AUTHOR: PRATT L F; RASSENTI L; LARRICK J; ROBBINS B; BANKS P M; KIPPS T J
AUTHOR ADDRESS: DEP. MOLECULAR EXPERIMENTAL MED., SCRIPPS CLINIC RES. FOUNDATION, LA JOLLA, CALIF. 92037.
JOURNAL: J IMMUNOL 143 (2). 1989. 699-705. **1989**
FULL JOURNAL NAME: Journal of Immunology
CODEN: JOIMA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Using the polymerase chain reaction we examined for specific Ig .kappa.-L chain V region gene (V.kappa. gene) rearrangement in small lymphocytic non-Hodgkin's lymphomas that express Ig bearing a major .kappa.-L chain associated cross-reactive Id, designated 17,109. Previously, we identified the 17.109-cross-reactive Id in chronic lymphocytic leukemia as a serologic marker for expression of a highly conserved V.kappa. gene, designated HumKv325. Using sense-strand

oligonucleotides specific for the 5'-end of this V.kappa. gene and **antisense** oligonucleotide specific for a J.kappa. region consensus sequence, we could amplify specifically Humkv325 when juxtaposed with J.kappa. through Ig gene rearrangement. This allowed us to amplify rearranged V.kappa. genes from DNA isolated from minute amounts of **lymphoma** biopsy material for molecular analyses. Our studies demonstrate that 17.109-reactive SL NHL, with or without associated CLL, rearrange, and presumably express, Humku325 without substanial somatic diversification. Our data suggest that malignant B cells in SL NHL, in contrast to NHL of follicular center cell origin, may express immunoglobulin variable region genes with little or no somatic hypermutation.

1989